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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/173,531	10/15/1998	Ralph M. Ellison	7409-150-999	1947

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EXAMINER	
PAK, JOHN D	
ART UNIT	PAPER NUMBER
1616	24

DATE MAILED: 09/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 09/173,531	Applicant(s) ELLISON ET AL.	
	Examiner JOHN D PAK	Art Unit 1616	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 14 August 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 5 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☐ The a)☐ affidavit, b)☐ exhibit, or c)☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: _____.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☒ Other: *See Continuation Sheet*

JOHN PAK
PRIMARY EXAMINER
GROUP 1600

Continuation of 3. Applicant's reply has overcome the following rejection(s): The grounds of rejection under 35 USC 103 and 35 USC 112 second paragraph.

Continuation of 10. Other: The Examiner has found three new abstracts of articles that require further review for patentability considerations relative to the cancer of the central nervous system, as presently claimed. Tne three abstracts are CAPLUS accession nos. 1994:648304, 1959:5256, and Medline accession no. 77108084. The amendment of 8/14/2003 will be entered. The FINALITY of th Office Action of 3/17/2003 (Paper No. 20) is hereby WITHDRAWN. A new Office Action will be prepared as soon as the full articles are obtained..

Attachments : the three above noted abstracts.

AN **1994:648304** CAPLUS
DN 121:248304
TI Comparative in vitro effects of sodium arsenite and sodium arsenate on neuroblastoma cells
AU Repetto, Guillermo; Sanz, Pilar; Repetto, Manuel
CS National Institute of Toxicology, P.O. Box 863, Sevilla, 41080, Spain
SO Toxicology (1994), 92(1-3), 143-53
CODEN: TXCYAC; ISSN: 0300-483X
PB Elsevier
DT Journal
LA English
AB The toxic effects of arsenic at different cellular levels were assessed using two inorg. chem. species: sodium arsenite and sodium arsenate, representing the trivalent and pentavalent states of arsenic, resp. Mouse neuroblastoma cell cultures (Neuro-2a) were exposed for 24 h, and cytotoxic effects evaluated were: cell proliferation by quantification of total protein content; cytoplasmic membrane integrity to cytosolic lactate dehydrogenase leakage; lysosomal hexosaminidase release; lactate dehydrogenase activity; mitochondrial succinate dehydrogenase activity; relative neutral red uptake by lysosomes; lysosomal hexosaminidase sphingolipid degrdn. activity; and acetylcholinesterase activity. As(III) was five times more toxic than As(V) to neuroblastoma cell proliferation, but the relative extent of other alterations differed. Special sensitivity was detected for lactate dehydrogenase inhibition. Hexosaminidase activity was also very susceptible, being inhibited at low concns. and stimulated at high concns. Less sensitive were the inhibition of cell proliferation, relative neutral red uptake, and acetylcholinesterase activity. As(III) was lysosomotropic, with secretion of hexosaminidase, but the release was decreased by As(V). Mitochondrial succinate dehydrogenase was inhibited by As(III) and stimulated by As(V). Minor sensitivity to cytoplasmic lactate dehydrogenase leakage for both compds. also shows that functional metabolic alterations produced by arsenic are more important than structural damage.

AN **1959:5256** CAPLUS
DN 53:5256
OREF 53:901d-f
TI The use of a rotating disk electrode in the study of electrochemical kinetics and electrolytic processes
AU Koutecky, J.; Levich, V. G.
CS Inst. Phys. Chem., Prague, Czech.
SO Zhurnal Fizicheskoi Khimii (1958), 32, 1565-75
CODEN: ZFKHA9; ISSN: 0044-4537
DT Journal
LA Unavailable
AB cf. C.A. 49, 1447e. Rotating disk electrodes were preferable to Hg drop electrodes in the study of reactions on electrodes involving kinetic and catalytic processes. The reactions on disk electrodes proceeded as stationary processes which permitted the formulation of reactions, even if they were complicated. Moreover, the properties of the solns. and the angular rotation velocities could be varied within wide limits with disk electrodes, while only the pH and the compn. of the soln. can be varied with the Hg drop electrode. The limiting diffusion currents were calcd. for typical cases on the assumption that the diffusion coeffs. (D) of the reacting substances were equal, because they frequently are very close. When D1 .noteq. D2, the calcns. are no more complex in principle but require longer computations.

AN **77108084** MEDLINE
DN 77108084 PubMed ID: 1243998
TI Immunological enhancement of chemotherapy in advanced brain cancer.
AU Rosner S
SO ACTA NEUROLOGICA LATINOAMERICANA, (1975) 21 (1-4) 126-32.
Journal code: 9421556. ISSN: 0001-6306.
CY Uruguay
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197703
ED Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19770321
AB Three hundred C3H mice were used to ascertain the validity of treatment of brain cancer with arsenicals and bacterial polysaccharide. It was found that this method of therapy was efficacious. Also, that a prophylactic effect was demonstrated. 2. In 14 patients with advanced intracranial neoplasm it was found: a) that no curative effect could be brought about once the cancer had spread beyond a certain point. This "point of no return" depends on tumor type, location and degree of brain destruction and general state of debility. b) That subjective and even some temporary objective improvement was possible even in advanced cancer. Necrosis of cancer tissue, that could be attributed to the therapy, was found in a number of cases. c) That some cases of brain cancer showed remarkable response to this form of therapy; more so if radiation therapy was given at the time of administration of the arsenical and bacterial polysaccharide. d) That some cases of brain metastasis showed "complete" destruction of the neoplasms in the brain although the patient subsequently died of the primary neoplasm and multiple metastasis. e) That the principle of enhancing the deposition of the curative material in the neoplasm by the use of bacterial polysaccharide is valid. f) That if this method of treatment (i.e. arsenical, bacterial polysaccharide and radiation) is instituted in the "early" cancer cases we may find it to be an efficacious mode of attack. g) That aresnical by mouth and bacterial polysaccharide by I.M. injection may be useful as a prophylactic to the formation of cancer. This may be contemplated for use in families that seem to show a predisposition to cancer formation. A mode of administration would probably be somewhat similary to the maintencance therapy described in the body of this paper. h) That bacterial polysaccharides have been shown to have the ability to destroy cancers.3,9 This method of enhancing the patients antigen-antibody reaction may eventually be used as a means of gaining an efficient vaccine in cancer therapy. i) Wherever possible definitive surgery should be carried out before the arsenical-bacterial polysaccharide-radiation method is instituted. j) In brain cancer, after craniotomy with removal of all or part of the neoplasm where feasible, the patient should be left with a subtemporal decompression. This will allow for the oedema of the brain that occurs with cerebral radiation therapy. k) That the principle of destruction of the cancer by certain special substances is valid. That the increase of affinity between cancer and destructive (curative) material can be brought about by administering a bacterial polysaccharide at the same time and that radiation therapy may enhance the beneficial effects of this method. 1) That the principle of brining the greatest toxicity to the cancer cells and the least toxic effect to the organism has been applied in the use of this method of treatment. m) That in some cases the cancer may not be destroyed by this therapy but may be made to retrogress or be held in check.